

**Remarks**

This RCE follows a Notice of Appeal filed in this case on May 4, 2009. The claims have been amended, canceling the previous claims 17, 83, 95, and 96. New claims 97-101 are added.

**Interview Summary**

Applicants thank the Examiner for the telephone interview conducted on June 25, 2009. Examiner Chung and Applicants attorneys Andrew Berks and Payam Moradian participated in the interview. At the interview, the Applicants discussed the proposed claim amendments and the support for these amendments in the specification. The Applicants distinguished the XRPD of Figs. 1 and 2. The absence of a melting enthalpy in the DSC curve of Fig. 3 was also noted. The Examiner indicated that claims to amorphous materials may be allowable if the claim referred to the XRPD pattern. The parties agreed that this RCE would be filed with amended claims. No prior art was discussed.

**New Claims**

Applicants are submitting new claims in this RCE, drawn to valsartan purely amorphous, which is recited in the original specification, on page 18, ll. 18–25. As noted in the specification, the purely amorphous valsartan of this invention is substantially free of crystalline structure, as shown by the XRPD and DSC data provided. The XRPD of valsartan purely amorphous, shown in Fig. 2 in this case, is a halo with no peaks or bumps in the regions characteristic of crystalline valsartan. The DSC for valsartan purely amorphous, shown in Fig. 3 in this case, shows no measurable melting enthalpy in the region of 80–140°C.

The inventive valsartan purely amorphous is distinguished from “valsartan essentially amorphous,” which is discussed in the instant application on page 18, ll. 8-16. XRPD patterns for valsartan essentially amorphous are shown in Fig. 1 of the instant application. It is readily apparent that the XRPD patterns of valsartan essentially amorphous have peaks or bumps around 6°, 15°, 18°, and 23° 2 $\theta$ . By contrast, the XRPD pattern of Fig. 2 is a smooth halo.

The new claims are fully supported by the three declarations previously submitted in this case. The Niddam-Hildesham and Koltai declarations, submitted on July 23, 2008, demonstrate that the prior art Buehlmyer disclosure did not produce valsartan purely amorphous, but rather produced amorphous valsartan with measurable crystalline contaminants. These conclusions were supported by the Desiraju declaration, submitted on February 19, 2009. Prof. Desiraju makes clear that the instant application has no measurable melting enthalpy at all. Desiraju declaration, para. 13. Prof. Desiraju further noted that a crystallographically impure material (such as “almost amorphous” valsartan) are undesirable pharmaceutical materials. Desiraju declaration, para. 14. This is because a material with partially amorphous and partially crystalline character would have mixed parameters resulting in inconsistent physical behavior, for example uneven and variable dissolution characteristics. *Id.*

Still further, Dr. Desiraju noted that the preparation of pure amorphous materials is not predictable. Desiraju declaration, para. 15. “Conventional techniques such as spray-drying, chromatography, and precipitation in solvent systems are not *a priori* dependable methods to prepare a pure amorphous or polymorphic material absent considerable experimentation.” *Id.*

Applicants further note that the term “halo” for the XRPD pattern of an amorphous material is a term of art. See, for example, J. K. Guillory, “Generation of polymorphs, hydrates, solvates, and amorphous solids,” in H.G. Brittain, (ed.) “Polymorphism in Pharmaceutical Solids,” (Marcel Dekker 1999), 183-219, at 208 (“amorphous materials exhibit the classical diffuse ‘halo’ x-ray powder diffraction pattern rather than the sharp peaks observed in the pattern of a crystalline substance.”). See also B.A. Sarsfield et al., ““Powder x-ray diffraction detection of crystalline phases in amorphous pharmaceuticals”, *Adv. X-Ray Anal.*, Vol. 49, 322-327 (2005) [http://www.icdd.com/resources/axa/vol49/V49\\_47.pdf](http://www.icdd.com/resources/axa/vol49/V49_47.pdf) (checked June 29, 2009), at 323 (“the expected PXRD pattern [of an amorphous API] will be an amorphous **halo**.”) (emphasis added).

## **Conclusion**

In view of the above remarks, the Applicants respectfully submit that the current claims are patentable over the prior art made of record in this case. Accordingly, an allowance of these claims is respectfully requested.

Respectfully submitted,

Dated: July 6, 2009

By: /Andrew H. Berks/  
Andrew H. Berks  
(Reg. No. 36,089)

KENYON & KENYON LLP  
One Broadway  
New York, NY 10004  
(212) 425-7200 (telephone)  
(212) 425-5288 (facsimile)

CUSTOMER NUMBER 26646